IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:		§	
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	Oron YACOBY-ZEEVI	§	
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Serial No.:	09/978,297	§	
		§	
Filed:	October 17, 2001	§	Group Art Unit: 1652
		§	
		§	
For:	Methods of and Pharmaceutical Compositions for Improving Implantation of Embryos	§	
		§	
		§	
		§	Attorney Docket: **01/22716**
		§	
Examiner:	Richard G. Hutson	§	

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 U.S.C. SECTION 1.131

Sir:

I, Dr. Iris Pecker, declare as follows:

1) I am the Iris Pecker who is an inventor related U.S. Application Ser. No. 09/776,874 (the '874 application).

2) I have analyzed the alignment data shown in Figure 17 of the '874 application. In my opinion, it provides ample guidance to the skilled artisan on how to make active heparanase variants. For example, residues 85 to 106 of human heparananse (SEQ ID NO:1 of the subject application) are identical to the corresponding residues of the variants shown in Figure 17. By contrast, for example, residues 23 to 36 have 11 residue differences. Similarly, comparing rat and human heparanase, residues 129 to 138, for example, have 8 differences among the 10 residues, with 9 of 10 differences among mouse and human at this region. With such guidance, the skilled artisan would know to not vary residues 85 to 106 and to vary one or more residues among residues 23 to 36 and/or 129 to 138, especially with a similar amino acid residue substitution (e.g., hydrophilic). The skilled artisan could even further use the guidance of the subject specification to replace one or more amino acid residues in SEQ ID NO:1, especially in these highly variable regions, with those corresponding residues found in mouse or rat heparanase.

3) Looking at heparanase protein more broadly, residues 49 to 109 make up 61 residues. Comparing mouse and human region at this region, there are only 10 of 61 changes. Comparing rat and human at this region, there are also only 10 of 61 changes. This is therefore a very conserved region, one that the skilled artisan would likely not vary, at least as a starting point, in trying to obtain additional heparanase homologs.

4) The conserved region of residues 49 to 109 was confirmed to be the 8 kDa unit of active heparanase. By contrast, variable regions 23 to 36 and 129 to 138, discussed in paragraph 2 above, are not part of either the small or large units of mature heparanase.

5) I have also reviewed an analysis of the heparanase taught by Fuks et al. (U.S. Pat. No. 5,362,641; hereinafter "Fuks"). This analysis shows that the heparanase of Fuks was inextricably mixed with a significant amount of at least six other proteins: PAI-1, Nexin-I, Vimentin, Grp94/endoplasmin, FLT receptor and Tryptase.

6) Indeed, the amount of these non-heparanase proteins present was so significant, that antibodies to one of these proteins (PAI-1) were elicited, while antibodies to heparanase could not be.

I declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willfully false statements are punishable by fine or imprisonment under 18 U.S.C. Section 1001 and that any such statement may jeopardize the validity of the subject application or any patent issued thereon.

Dr. Iris Pecker

12/1/06
Date